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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/522,753	03/10/2000	Ronald M. Evans	SALK1510-3	4924

30542 7590 09/22/2006

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 09/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/522,753	EVANS ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/20/2005, 1/17/2006 and 5/25/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-5,14,16 and 18-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-5,14,16 and 19-25* is/are rejected.

7)☒ Claim(s) *18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Exhibits I-XI*.

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 9/20/2005, in which claims 1-2, 6-8, 11, 15 and 26-37 were canceled, and claims 5, 14, and 16 were amended. Receipt is also acknowledged of an amendment, filed 1/17/2006 in which claims 1-2, 6-13, 15, 17 and 26-38 were canceled, and claims 14 and 16 were amended. Currently, claims 3-5, 14, 16 and 18-25 are pending in the present application.

Any rejection of record in previous office actions not addressed herein is withdrawn. This action is not final due to new grounds of rejection made herein that were not necessitated by applicants' amendment of the claims in the responses filed 9/20/2005 and 1/17/2006.

Election/Restrictions

Applicant's election with traverse of Group I (claims 3-5, 14, 16 and 18-25, as they read on SEQ ID NOS: 4 and 5) in the reply filed on 1/17/2006 is acknowledged. The traversal is on the ground(s) that all of the claims are interrelated such that a search of the prior art of one group would uncover art of potential relevance to the other groups, and thus there would be no undue burden to the examiner to search additional groups. Further, the response asserts that the MPEP provides for the search of up to 10 sequences without restriction. This is not found persuasive because each group requires separate searches of the commercial sequence databases. To search the commercial sequence databases for the sequences of more than one group would impose a serious search burden. Additional computer time is required for each sequence search. There is a very high and undue burden for examining more than one sequence as a result of the continual exponential increase of size of the sequence databases. While the MPEP provides for the search

of up to ten sequences, the length of the claimed sequences precludes the search of more than the sequences of the elected group. The search of more than one group cannot be completed due to the excess computer time required for searching. Further, the search of more than one sequence would require additional time to review the computer search results. Moreover, a single search of the commercial sequence databases is insufficient to determine if the prior art sequences meet each of the limitations of the claims. For example, claim 3 requires a second sequence comparison with instant SEQ ID NO: 11. Therefore, the search of more than the elected group would impose a serious search burden.

The requirement is still deemed proper and is therefore made FINAL.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). The prior application to which the instant application seeks priority is U.S. Application Serial No. 08/522,726, filed 9/1/1995 (now U.S. Patent No. 6,489,441). The '726 application discloses only 3 sequences that correspond to SEQ ID NOS: 1-3 of the instant application. Each of the pending claims is directed to an isolated polynucleotide

that (i) has a recited percent identity to one of SEQ ID NOS: 4, 6, & 8; or (ii) encodes a polypeptide having a recited percent identity to one of SEQ ID NOS: 5, 7 & 9. The prior application does not disclose these particular sequences. Therefore, the prior application does not provide support for the broadly recited genus of polynucleotides encompassed by the pending claims. Accordingly, the priority date for the pending claims is the filing date of the instant application (3/10/2000).

Applicant's arguments filed 9/20/2005 have been fully considered but they are not persuasive. The response asserts that the prior application discloses co-suppressors of steroid/thyroid hormone receptor activity having defined amino acid residues, or conservative variations thereof, and that the present application properly claims priority because the human SMRT sequence disclosed in the present application is an extension of the sequence information disclosed in the parent application. The response notes that the present application includes "newly discovered SMRT sequence information." Further, the response asserts that the sequence information disclosed in the parent application, and disclosed and claimed in the present application that is entitled to the priority date of the parent application. This is not found persuasive because the instant claims encompass sequences not disclosed in the parent application. Thus, the sequences of the parent application do not provide support under 35 USC 112, first paragraph, for the full scope of any of the present claims. As discussed above, the parent application does not disclose SEQ ID NOS: 4 and 5. Thus, the effective filing date of the present claims is 3/10/2000.

Specification

The disclosure is objected to because of the following informalities: the status of US Application Numbers08/522,726 and 09/523,068 should be updated to read "now US Patent No. 6,489,441" and "now abandoned," respectively (See the paragraph beginning at line 7 of page 1).

Appropriate correction is required.

Response to Amendment

The declaration under 37 CFR 1.132 filed 9/20/2005 is sufficient to overcome the rejection of claims 4, 19, 21-22 based upon Ordentlich et al (PNAS USA, 16 March 1999, Vol. 96, No. 6, pages 2639-2644) reference applied under 35 U.S.C. 102(a).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3-5 and 19-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al (Nature, October 1995, Vol. 377, No. 6548, pages 454-457, cited in a prior action; see the entire reference). This rejection was made in the Office action mailed 5/23/2005 and has been extended to include additional claims, which was not necessitated by Applicant's amendment to the claims filed on 9/20/2005 or 1/17/2006. Thus, this is a new rejection.

Chen et al teach the identification and characterization of a transcriptional co-repressor that is a SMRT (i.e. silencing mediator for retinoid and thyroid hormone receptors). The SMRT polypeptide taught by Chen et al is encoded by a polynucleotide sequence that encodes a polypeptide that is ~94% identical to the sequence of SEQ ID NO: 5 (see Exhibit A, result #6 for accession number HSU37146, mailed 5/23/2005). The nucleotide sequence of HSU37146, encodes a protein that has less than 83% identity with a Sin3A interaction domain of N-CoR as set forth as amino acids 255 to 312 of SEQ ID NO: 11, has less than about 57% identity with the repression domain 1 of N-CoR set forth as amino acids 1 to 312 of SEQ ID NO: 11, has less than about 66% identify with a SANT domain of N-CoR set forth as amino acids 312 to 668 of SEQ ID NO: 11, and has less than bout 30% identity with repression domain 2 of N-CoR set forth as amino acids 736-1031 of SEQ ID NO: 11 (see Exhibits I-VI, where the amino acid sequence of HSU37146 (AAC50236.1) is compared to the claimed regions of human N-CoR as set forth in O75376, which is 100% identical to instant SEQ ID NO: 11). Further, Chen et al teach a plasmid comprising a nucleic acid sequence encoding a SMRT-GAL4 DNA binding domain fusion protein (e.g. paragraph bridging pages 456-457; Figure 4). Thus, the polynucleotide sequence taught by Chen et al anticipates the broad genus of polynucleotides encompassed by the instant claims.

Claims 3-5, 14 and 19-22 are rejected under 35 U.S.C. 102(a) as being anticipated by Park et al (PNAS USA, 30 March 1999, Vol. 96, No. 7, pages 3519-3524, cited in a prior action; see the entire reference). This rejection was made in the Office action mailed 5/23/2005 and has

been extended to additional claims, which was not necessitated by Applicant's amendment to the claims filed on 9/20/2005 or 1/17/2006. Thus, this is a new rejection.

Park et al teach the identification of an extended isoform of SMRT termed SMRTe by the authors. In particular, Park et al teach nucleic acids, described by accession numbers AF125672 & AF125671, that encode polypeptides with ~98% and ~82% identity with SEQ ID NO: 5 (e.g. see results 2 & 4 of the search report provided as Exhibit A, mailed 5/23/2005). The nucleic acid sequence of AF125672 encodes a protein with 63% identity to amino acids 1-312 of SEQ ID NO: 11 (see Exhibit I). The nucleic acid sequence of AF125671 encodes a protein with 56% identity to amino acids 1-312 of SEQ ID NO: 11 and 60% identity to amino acids 312-668 of SEQ ID NO: 11 (see Exhibits VII & VIII, respectively). Further, the nucleic acid sequence of AF125672 is 97% identical to the nucleic acid sequence of SEQ ID NO: 4 (see Exhibit IX). Moreover, the nucleic acid sequence of AF125672 is 98% identical to nucleotides 1-3094 of SEQ ID NO: 4 (see Exhibit X). Park et al teach a polynucleotide comprising a sequence encoding the N-terminal sequence of SMRTe (aa 1-1111) operatively linked to a Gal4 DNA binding domain in a plasmid expression construct, which was transfected into HeLa cells to determine assay repression activity (e.g. page 3522, left column, 2nd paragraph; page 3520, left column, 1st full paragraph; page 3524, left column, 1st paragraph; Figure 3). Further, Park et al teach the SMRTe nucleic acid sequence in the pBluescript vector (e.g. paragraph bridging pages 3519-3520).

Claims 23 and 25 are rejected under 35 U.S.C. 102(a) as being anticipated by GenBank Accession Number NM_002900.1 (GI: 4506452, 3/19/1999). This is a new rejection.

GenBank Accession Number NM_002900.1 teaches a nucleotide sequence that contains a sequence of at least 15 nucleotides (nt 2861-2847) that is 100% identical to nucleotides 1-15 of instant SEQ ID NO: 4 (See Exhibit XI). This sequence will hybridize to a polynucleotide of claim 4 without hybridizing to a polynucleotide that encodes SEQ ID NO: 11 or a polynucleotide that encodes SEQ ID NO: 9.

Response to Arguments - 35 USC § 102

Applicant's arguments, see page 9 of 12, filed 9/20/2005, with respect to the rejection of claims 4, 19 and 21-22 under 35 U.S.C. 102(a) as being anticipated by Ordentlich et al (PNAS USA, 16 March 1999, Vol. 96, No. 6, pages 2639-2644) have been fully considered and are persuasive. The previous rejection of claims 4, 19 and 21-22 has been withdrawn.

With respect to the rejection of claims 4, 19 and 21-22 under 35 U.S.C. 102(a) as being anticipated by Park et al (PNAS USA, 30 March 1999, Vol. 96, No. 7, pages 3519-3524), Applicant's arguments filed 9/20/2005 have been fully considered but they are not persuasive. The response asserts that Park et al merely published similar findings to those reported by Ordentlich et al, only two weeks later. The response asserts that the earlier publication of Ordentlich et al clearly demonstrates that Applicants were in possession of the present invention before the effective date of the Park publication. This is not found persuasive because the sequences disclosed in the Ordentlich and Park references are not identical. The sequences disclosed by Ordentlich et al are not sufficient to describe the broadly claimed genus. The sequences disclosed by Park et al are not obvious variants of the sequences disclosed by

Ordentlich et al. Thus, the Ordetlich reference does not provide evidence that Applicant's were in possession of the invention disclosed by Park et al prior to the date of the Park reference.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

With respect to the rejection of claims 4, 19 and 21-22 under 35 U.S.C. 102(b) as being anticipated by Chen et al (Nature, October 1995, Vol. 377, No. 6548, pages 454-457), Applicant's arguments filed 9/20/2005 have been fully considered but they are not persuasive. The response asserts that Applicants are entitled to a priority date of September 1, 1999, for at least the portion of SEQ ID NO: 5 that is disclosed in the parent application. The response indicates that SEQ ID NO: 1 of the parent application provides support for a portion of instant SEQ ID NO: 5. The response notes that the parent application was based on the Chen publication, which discloses the human SMRT sequence disclosed and claimed in the parent application. MPEP 706.02(V) states the following with regard to determining the effective filing date of an application:

> If the application is a continuation-in-part of an earlier U.S. application or international application, any claims in the new application not supported by the specification and claims of the parent application have an effective filing date equal to the filing date of the new application. Any claims which are fully supported under 35 U.S.C. 112 by the earlier parent application have the effective filing date of that earlier parent application.

In the instant case, the claims are **not fully supported** by the specification of the 08/522,726 application. The instant claims encompass sequences other than those disclosed in the parent application. Thus, the effective filing date is that of the present application (3/10/2003). The Chen et al reference was published more than one year prior to 3/10/2003. Therefore, the

reference qualifies as prior art under 35 U.S.C. 102(b) and is properly applied under 35 U.S.C. 102(b).

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection was made in the Office action mailed 5/23/2005 and has been rewritten below.

This is a new matter rejection.

Claim 23 is directed to a genus of oligonucleotides that are identifiable under "suitable stringency conditions" with respect to other nucleic acid sequences. The term "suitable stringency conditions" is used in the context of an identified oligonucleotide comprising at least 15 nucleotides that hybridizes to a polynucleotide of claim 4, but not to a polynucleotide encoding SEQ ID NO: 11 or to a polynucleotide encoding an amino acid sequence consisting of amino acids 1031 to 2517 of SEQ ID NO: 5. The specification lacks antecedent basis for this term and does not define these exact conditions and the skilled artisan has no basis to visualize

what these "suitable" conditions might be. Similarly, claim 25 specifies that the oligonucleotide of claim 23 hybridizes under "suitable stringency conditions" to a polynucleotide encoding SEQ ID NO: 5 or SEQ ID NO: 7, but does not hybridize to a polynucleotide encoding SEQ ID NO: 9. Again, the exact hybridization conditions are not described. Thus, the rejected claims comprise a genus of oligonucleotides that must meet very particular hybridization requirements, yet there is no description of the hybridization conditions that will necessarily identify an oligonucleotide having the recited functional activity.

Claim 23 is directed to a genus of oligonucleotides that hybridize to the polynucleotide of claim 4, but does not hybridize to "a polynucleotide encoding an amino acid sequence consisting of amino acids 1031 to 2517 of SEQ ID NO: 5." The specification does not provide literal or inherent support for the exclusion of this sub-genus of oligonucleotides.

At page 17, lines 16-28, the specification envisions the following with regard to oligonucleotides:

> Additional examples of invention isolated oligonucleotides, are those which generally are at least about 15 nucleotides in length and can hybridize specifically to the polynucleotide of the invention, but not to a polynucleotide encoding an N-CoR polypeptide (SEQ ID NO: 11). An oligonucleotide of the invention can be useful as a probe, or as a primer for a PCR procedure, or can encode a peptide containing at least five contiguous amino acids of a SMRT co-repressor. In one embodiment, an oligonucleotide of the invention encodes at least five contiguous amino acids of a sequence such as that shown as amino acids 720 to 745 of SEQ ID NO: 5, or amino acids 716 to 742 of SEQ ID NO: 7; or amino acids 497 to 523 of SEQ ID NO: 9. In another embodiment, an oligonucleotide of the invention can hybridize specifically to a polynucleotide encoding human SMRT (SEQ ID NO: 5) or mouse SMRTα (SEQ ID NO: 7), and, optionally, to a polynucleotide encoding mouse SMRTβ (SEQ ID NO: 9).

There does not appear to be any literal or implicit support in the originally filed claims or specification for claiming an isolated oligonucleotide comprising at least 15 nucleotides and

having the particular hybridization characteristics recited in the rejected claims (i.e. that hybridized under "suitable stringency conditions") or excludes oligonucleotides that do not hybridize to "a polynucleotide encoding an amino acid sequence consisting of amino acids "1031 to 2517 of SEQ ID NO: 5." Therefore, the rejected claims comprise impermissible NEW MATTER.

Claims 23-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new rejection.

The claims are drawn to a genus of oligonucleotide comprising at least 15 nucleotides that must meet specific functional limitations of the claims. The claims require the oligonucleotides to be capable of performing the following functions: (i) hybridizing "under suitable stringency conditions" to the polynucleotide of claim 4, which is a polynucleotide that encodes a SMRT co-repressor, or peptide portion thereof, wherein said SMRT co-repressor or portion thereof is capable of mediating transcriptional silencing and has a sequence at least 80% identical with SEQ ID NO: 5, and (ii) does not hybridize to a polynucleotide encoding SEQ ID NO: 11 or to a polynucleotide encoding an amino acid sequence consisting of amino acids 1031 to 2517 of SEQ ID NO: 5. Thus, the genus of oligonucleotides must be capable of hybridizing to a genus of polynucleotides defined by function and the ability to encode a protein at least 80% identical to SEQ DI NO: 5, while not being able hybridize to a genus of polynucleotides defined

by the ability to encode the protein of SEQ ID NO: 11. The polynucleotides that encode the amino acid sequence of SEQ ID NO: 11 are many due to the degeneracy of the genetic code. Claim 24 further requires that "the polynucleotide" encodes at least five contiguous amino acids of a sequence of amino acids 720-745 of SEQ ID NO: 5. It is unclear whether this is limiting the polynucleotide of claim 4 or the sequence of the oligonucleotide. Claim 25 further requires that the oligonucleotide hybridize to a genus of polynucleotides encoding SEQ ID NO: 5 without hybridizing to a genus of polynucleotides encoding SEQ ID NO: 9. Thus, he rejected claims thus comprise a set of oligonucleotides that encompass specific functional limitations with regard to the ability to hybridize to one genus of sequences without hybridizing to another.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. At page 17, lines 16-28, the specification envisions the following with regard to oligonucleotides:

> Additional examples of invention isolated oligonucleotides, are those which generally are at least about 15 nucleotides in length and can hybridize specifically to the polynucleotide of the invention, but not to a polynucleotide encoding an N-CoR polypeptide (SEQ ID NO: 11). An oligonucleotide of the invention can be useful as a probe, or as a primer for a PCR procedure, or can encode a peptide containing at least five contiguous amino acids of a SMRT co-repressor. In one embodiment, an oligonucleotide of the invention encodes at least five contiguous amino acids of a sequence such as that shown as amino acids 720 to 745 of SEQ ID NO: 5, or amino acids 716 to 742 of SEQ ID NO: 7; or amino acids 497 to 523 of SEQ ID NO: 9. In another embodiment, an oligonucleotide of the invention can hybridize specifically to a polynucleotide encoding human SMRT (SEQ ID NO: 5) or mouse SMRTα (SEQ ID NO: 7), and, optionally, to a polynucleotide encoding mouse SMRTβ (SEQ ID NO: 9).

No description is provided of any oligonucleotide that meets the functional limitations of the claims. Given the related nature of the N-CoR protein of SEQ ID NO: 11 and the SMRT co-repressor of SEQ ID NO: 5, one cannot envision those oligonucleotides that would be capable of hybridizing to polynucleotides of claim 4 without hybridizing to the polynucleotides encoding SEQ ID NO: 11.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of oligonucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Given the very large genus of oligonucleotides encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to the specific nucleotide sequences that one could use to design oligonucleotides that meet the functional limitations of the claims, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the broadly claimed genus of oligonucleotides. Thus, there is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision those oligonucleotides that satisfy the functional limitations of the claims. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention for claims 23-25.

Claims 14 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides encoding a SMRT co-repressor, where the polynucleotide comprises a nucleotide sequence having at least 80% sequence identity with nucleotides 1 to 3094 of SEQ ID NO: 4, does not reasonably provide enablement for complements of these nucleotide sequences, which also must encode a SMRT co-repressor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is a new rejection.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of

experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The claims are drawn to polynucleotides that encode a SMRT co-repressor, or a peptide portion thereof, wherein the SMRT co-repressor or peptide portion thereof is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors. Claim 14 is drawn to a polynucleotide comprising a nucleotide sequence having at least 80% sequence identity with nucleotides 1 to 3094 of SEQ ID NO: 4, and a polynucleotide complementary thereto. The complementary polynucleotide cannot contain "a sequence" identical to SEQ ID NO: 11. Thus, the claimed sequence cannot have 2 or more contiguous nucleotides in common with SEQ ID NO: 11. Claim 16 is drawn to a polynucleotide comprising nucleotides 1 to 3094 of SEQ ID NO: 4, and a polynucleotide having 80% sequence identity with the complementary sequence of nucleotides 1 to 3094 of SEQ ID NO: 4. The nature of the invention is complex in that all of the claimed polynucleotides must encode a SMRT co-repressor or peptide portion thereof with a specific functional activity.

Breadth of the claims: The claims are broad in that they are drawn to coding sequences and complements thereof. The breadth of the claims exacerbates the complex nature of the subject matter of this invention.

Guidance of the specification and existence of working examples: The specification teaches that the polynucleotide of SEQ ID NO: 4 encodes a human SMRT co-repressor (SEQ ID NO: 5; e.g. page 9, lines 15-22). The specification teaches that the N-terminal region of the protein encoded by SEQ ID NO: 4 can modulate the transcriptional potential of a nuclear

receptor, particularly a nuclear receptor that is in the form of a dimer, for example, a thyroid hormone receptor homodimer, a retinoic acid receptor homodimer, a retinoid X receptor homodimer, etc. (e.g. paragraph bridging pages 9-10). Specifically, amino acids 1-1031, 1-303 and 736-1031, and the SANT domain of SEQ ID NO: 5 confer a significant amount of repression (e.g. Example 11). Based upon the teachings of the specification, it is within the skill of the art to use the nucleotide sequence of SEQ ID NO: 4, or a nucleotide sequence having at least 80% sequence identity to SEQ ID NO: 4 to encode a protein with nuclear hormone repression activity (e.g. Figure 9).

Predictability and state of the art: It would be unpredictable to make and use the claimed invention because the coding strand and complement to the coding strand will not encode the same protein. For example, a nucleotide sequence of 5'- CCC CCC CCC -3' encodes a peptide of ProProPro, whereas the complement 5' GGG GGG GGG -3' encodes a peptide of GlyGlyGly. Thus, complementary strands of nucleic acid molecules do not normally have the same coding potential.

Amount of experimentation necessary: The quantity of experimentation necessary to carry out the claimed invention is high as the skilled artisan could not rely on the prior art or the present specification to teach how to make and use any nucleic acid that encode a polypeptide having SMRT co-repressor activity and is also complementary to a polynucleotide encoding a protein having SMRT co-repressor activity. In order to carry out the claimed invention, one would have to determine if coding and non-coding strands of a double stranded nucleic acid molecule could be constructed such that they meet the structural and functional requirements of claims 14 and 16. First, one would have to identify all sequences that are 80% identical to SEQ

ID NO: 4. Next, one would have to identify all complementary nucleic acids to the nucleic acids identified in the first step. Finally, one would have to test each of the nucleic acids for the ability to encode proteins having SMRT co-repressor activity. Furthermore, any polynucleotide containing "a nucleic acid sequence" (i.e. two or more nucleotides) of SEQ ID NO: 11 would be excluded. The likelihood of one being able to make a nucleic acid that meets each of the limitations of the claims is exceedingly low.

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an undue amount of experimentation to make and/or use the claimed invention. Therefore, claims 14 and 16 are not considered to be fully enabled by the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 14, 16 and 23-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection was made in the Office action mailed 5/23/2005 and has been rewritten to address the amendments to the claims, filed 1/17/2006 and has been extended to claim 3.

Claim 3 is vague and indefinite in that the metes and bounds of the term "less than about" are unclear. The term is unclear in that it refers to a percent identity with a particular portion of N-CoR. It is unclear if the polynucleotide must encode a protein with less than the specified

percent identity or whether the claims encompass protein with more than the specified percent identity.

Claim 14 recites "an isolated polynucleotide encoding a SMRT co-repressor" and then recites that the polynucleotide is selected from a Markush group of different polynucleotides. It is unclear how the polynucleotides of part (b) can encode a SMRT co-repressor, or portion thereof, when they are *complementary* to sequences in part (a) that actually do encode an SMRT co-repressor. Similarly, claim 16 also recites that the polynucleotides of part (b) have 80% identity to the *complement* of sequences in part (a). It is unclear how the polynucleotides of part (b) of claim 16 can encode a SMRT co-repressor, or portion thereof, when they are *complementary* to nucleotides 1 to 3094 of SEQ ID NO: 4. Furthermore, the phrase "provided that the polynucleotide does not contain a sequence identical to SEQ ID NO: 11" is vague and indefinite in that it is unclear if the phrase refers to the polynucleotide encoding the SMRT co-repressor, or the polynucleotide complementary to the coding sequence, or both.

Claim 23 is vague and indefinite in that the metes and bounds of the phrase "suitable stringency conditions" are unclear. The phrase is used in the context of an identified oligonucleotide comprising at least 15 nucleotides that hybridizes to a polynucleotide of claim 4, but not to a polynucleotide encoding SEQ ID NO: 11 or to a polynucleotide encoding an amino acid sequence consisting of amino acids 1031 to 2517 of SEQ ID NO: 5. The use of "suitable stringency conditions" renders the claim(s) vague and indefinite, because there is no clear art-recognized definition for the term, and the specification fails to set forth a clear definition. Thus the metes and bounds of the conditions encompassed by the term are unclear.

Claim 24 depends from claim 23, and thus is indefinite for the same reasons as applied to claim 23. Similarly, claim 25 specifies that the oligonucleotide of claim 23 hybridizes under "suitable stringency conditions" to a polynucleotide encoding SEQ ID NO: 5 or SEQ ID NO: 7, but does not hybridize to a polynucleotide encoding SEQ ID NO: 9.

Claim 24 is vague and indefinite in that the metes and bounds of the phrase "wherein the polynucleotide encodes at least five contiguous amino acids" of amino acids 720 to 745 of SEQ ID NO: 5 are unclear. The phrase is unclear in that claim 24 depends from claim 23, which recites a "polynucleotide encoding SEQ ID NO: 11" and "a polynucleotide encoding an amino acid sequence consisting of amino acids 1031 to 2517 of SEQ ID NO: 5" and depends from claim 4 which is drawn to a polynucleotide capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors and having at least 80% sequence identity with SEQ ID NO: 5. Furthermore, an oligonucleotide is a polynucleotide. Thus, it is unclear which polynucleotide of the claim must encode at least five contiguous amino acids of amino acids 720-745 of SEQ ID NO: 5. It would be remedial to amend the claim language to clearly indicate which polynucleotide is being further limited.

Response to Arguments - 35 USC § 112

Applicant's arguments, see page 10 of 12, filed 9/20/2005, with respect to the rejection of claims 5 and 18 under 35 U.S.C. 112, first paragraph have been fully considered and are persuasive. The previous rejection of claims 5 and 8 has been withdrawn.

Applicant's arguments, see page 11 of 12, filed 9/20/2005, with respect to the rejection of claims 5 and 18 under 35 U.S.C. 112, second paragraph, have been fully considered and are persuasive. The previous rejection of claims 5 and 18 has been withdrawn.

With respect to the rejection of claims 14 and 16 under 35 U.S.C. 112, second paragraph, Applicant's arguments filed 9/20/2006 have been fully considered but they are not persuasive. The response asserts that the claims have been amended to make it clear that the claimed polynucleotide embraces both the coding sequence (first nucleotide) and complement thereto (second nucleotide), and thus the nucleotide of part (d) of the claim would not be required to encode a SMRT co-repressor. This is not found persuasive, because the claims are drawn to a single isolated polynucleotide that must encode a SMRT co-repressor that is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors. Part (d) of the claim is now part (b), and still requires the complement of a SMRT coding sequence to encode a SMRT protein. For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

With respect to the rejection of claims 23-25 under 35 U.S.C. 112, second paragraph, Applicant's arguments filed 9/20/2006 have been fully considered but they are not persuasive. The response asserts that one of skill in the art could readily identify "suitable" conditions to accomplish the desired goal. This is not found persuasive, because there is no clear art-recognized definition for the term, and the specification fails to set forth a clear definition. Thus the metes and bounds of the conditions encompassed by the term are unclear. For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Conclusion

No claims are allowed.

Claim 18 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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PRIMARY EXAMINER